1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Therios 750 mg palatable tablets for dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance:
Each tablet contains:
Cefalexin (as cefalexin monohydrate).....750 mg

Excipients:

Qualitative composition of excipients and other constituents
Croscarmellose sodium
Silica, colloidal anhydrous
Magnesium stearate
Yeast dried
Biscuit flavour F07012
Ammonium glycyrrhizate
Macrogol 6000

Round scored beige palatable tablet.
The tablet can be divided into halves and quarters.

3. CLINICAL INFORMATION

3.1 Target species

Dogs.

3.2 Indications for use for each target species

For the treatment of bacterial skin infections in dogs (including deep and superficial pyoderma) caused by organisms sensitive to cefalexin.
For the treatment of urinary tract infections in dogs (including nephritis and cystitis) caused by organisms sensitive to cefalexin.

3.3 Contraindications

Do not use in cases of hypersensitivity to penicillins, cephalosporins or to any the excipients.
Do not use in case of severe renal failure.
Do not use in rabbits, guinea pigs, hamsters and gerbils.

3.4 Special warnings

None.

3.5 Special precautions for use

Special precautions for safe use in the target species:

Wherever possible, the use of the veterinary medicinal product should be based on susceptibility testing and take into account official and local antimicrobial policies.

As with other antibiotics which are excreted mainly by the kidneys, systemic accumulation may occur when renal function is impaired. In case of known renal insufficiency the dose should be reduced.
The veterinary medicinal product is not recommended for use in dogs less than 6 kg bodyweight.

Use of the veterinary medicinal product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to cefalexin and may decrease the effectiveness of treatment with other beta-lactam antibiotics due to the potential for cross-resistance.

Safety of the excipient, ammonium glycyrrhizate, has not been established in dogs less than 1 year old.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:

Cephalosporins may cause sensitisation (allergy) following injection, inhalation, ingestion or skin contact. Sensitivity to penicillins may lead to cross sensitivity to cephalosporin and vice versa. Allergic reactions to these substances may occasionally be serious.
1. People with known hypersensitivity to cephalosporins should avoid contact with the veterinary medicinal product.
2. Handle this veterinary medicinal product with great care to avoid exposure, taking all recommended precautions. Wash hands after use.
3. If you develop symptoms following exposure such as skin rash you should seek medical advice and show the doctor this warning. Swellings of the face, lips or eyes or difficulty breathing are more serious symptoms and require urgent medical attention.

In case of accidental ingestion, particularly by a child, seek medical advice immediately and show the package leaflet or the label to the physician.

Special precautions for the protection of the environment:
Not applicable.

3.6 Adverse events

Dogs:

Rare	Hypersensitivity reaction

(1 to 10 animals / 10,000 animals treated):	
Undetermined frequency (cannot be estimated from the available data):	Vomiting, Diarrhoea

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or the national competent authority via the national reporting system. See the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

Pregnancy and lactation:
Do not use during pregnancy or lactation.

3.8 Interaction with other medicinal products and other forms of interaction

In order to ensure efficacy, the veterinary medicinal product should not be used in combination with bacteriostatic antibiotics.
Concurrent use of first generation cephalosporins with aminoglycoside antibiotics or some diuretics such as furosemide can enhance nephrotoxicity risks.

3.9 Administration routes and dosage

Oral use.

15 mg cefalexin per kg bodyweight twice daily (equivalent to 30 mg per kg bodyweight per day) for duration of:
- 14 days in cases of urinary tract infection.
- At least 15 days in cases of superficial infectious dermatitis.
- At least 28 days in cases of deep infectious dermatitis.

In severe or acute conditions the dose may be safely doubled to 30 mg/kg twice daily.
To allow for accuracy of dosing, tablets can be halved or quartered.

Any increase in the dose or duration of treatment should be according to a risk/benefit assessment by the prescribing veterinarian.

To ensure a correct dosage bodyweight should be determined as accurately as possible.

The veterinary medicinal product is well accepted by dogs but may be crushed or added to a small quantity of food immediately prior to feeding if necessary.

3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

Trials performed on animals with up to 5 times the recommended twice daily dosage of 15 mg/kg demonstrated that cefalexin was well tolerated.

3.11. Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance

Not applicable.

3.12 Withdrawal periods

Not applicable.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code:

QJ01DB01

Cefalexin monohydrate, the active ingredient of the Therios tablets, is a bactericidal antibiotic of the cephalosporin family, obtained by hemi-synthesis of the 7 amino-cephalosporanic nucleus.

4.2 Pharmacodynamics

Cefalexin acts by inhibiting the nucleopeptide synthesis of the bacterial wall. Cephalosporins interfere with transpeptidation by acylating the enzyme making it unable to cross-link muramic acid-containing peptidoglycan strands. The inhibition of the biosynthesis of the material required to build the cell wall results in a defective cell wall and consequently osmotically unstable to protoplasts. The combined action results in cell lysis and filament formation.
Cefalexin is active against Gram positive pathogens such as Streptococcus spp. and Staphylococcus spp. (including penicillin-resistant strains) and Gram negative pathogens such as Proteus mirabilis and some strains of Escherichia coli and Klebsiella spp.
Cefalexin is active against Methicillin-susceptible staphylococci including penicillin-resistant strains not against Methicillin-resistant staphylococci.

Cefalexin is active against most beta-lactamase-producing Gram positive bacteria and has moderate activity against certain non-transferable (chromosomal) beta-lactamase-producing Gram negative Enterobacteriaceae and fastidious Gram negatives.
Resistance is plasmid-mediated or transmitted by chromosomal route.

Cefalexin has a time-dependent bactericidal activity against *Staphylococcus* spp. and *Pasteurella multocida*.

CLSI cefalexin veterinary breakpoints are available for dogs in *Staphylococcus aureus*, *Staphylococcus pseudintermedius,* Streptococci-β-hemolytic group and *Escherichia coli* in skin and soft tissue infections. (CLSI, July 2013).

- Susceptible: ≤ 2 ug/mL
- Resistant: ≥ 8 ug/mL

Resistance to cefalexin may be due to one of the following mechanisms of resistance. Firstly, the production of various beta-lactamases (cephalosporinase), that inactivate the antibiotic, is the most prevalent mechanism among gram-negative bacteria. Secondly, a decreased affinity of the PBPs (penicillin-binding proteins) for beta-lactam drugs is frequently involved for beta-lactam resistant gram-positive bacteria. Lastly, efflux pumps, extruding the antibiotic from the bacterial cell, and structural changes in porins, reducing passive diffusion of the drug through the cell wall, may contribute to improve the resistant phenotype of a bacterium.

Well-known cross-resistance (involving the same resistance mechanism) exists between antibiotics belonging to the beta-lactam group due to structural similarities. It occurs with b-lactamases enzymes, structural changes in porins or variations in efflux pumps. Co-resistance (different resistance mechanisms involved) has been described in *E. coli* due to a plasmid harbouring various resistance genes.

4.3 Pharmacokinetics

After single oral administration of the recommended dosage of 15 mg cefalexin per kg bodyweight to Beagle dogs, plasma concentrations were observed within 30 minutes. The plasma peak was observed at 1.33 hours with a plasma concentration of 21.2 µg/ml. The bioavailability of the active was over 90%. Cefalexin was detected until 24 hours after the administration. The first urine specimen was collected within 2 to 12 hours with peak concentrations of cefalexin measured at 430 to 2758 µg / ml within 12 hours.
After repeated oral administration of the same dosage, twice a day for 7 days, plasma peaks occurred 2 hours later with a concentration of 20 µg/ml. Over the treatment period concentrations were maintained above 1 µg/ml. The mean elimination half-life is 2 hours. Skin levels were around 5.8 to 6.6 µg /g 2 hours after treatment.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

Not applicable.

5.2 Shelf life

Shelf-life of the veterinary medicinal product as packaged for sale: 3 years.
Shelf-life after first opening the immediate packaging: 48 hours.
Any divided tablet portions remaining after 48 hours should be discarded.

5.3 Special precautions for storage

Do not store above 25°C.
Divided tablets should be stored in the blister pack.

5.4 Nature and composition of immediate packaging

Polyvinylchloride blister heat sealed with an aluminium cover foil.

Pack sizes:
Cardboard box with 1 blister of 10 tablets.
Cardboard box with 3 blisters of 10 tablets.
Cardboard box with 20 blisters of 10 tablets.

Not all pack sizes may be marketed.

5.5 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products

Medicines should not be disposed of via wastewater or household waste.
Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

Ceva Santé Animale

7. MARKETING AUTHORISATION NUMBER(S)

VPA10815/033/003

8. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

16/04/2010

9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

06/11/2024

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.
Detailed information on this veterinary medicinal product is available in the Union Product Database.
(https://medicines.health.europa.eu/veterinary)